IMPROVING GLYCOSYLATION PROFILES AND CELL CULTURE PERFORMANCE WITH A SENSITIVE CELL LINE IN COMMERCIAL MANUFACTURING

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A history of sporadically poor culture performance in the inoculum train and subsequent production cultures has been observed in a CHO cell line expressing a recombinant mAb X, resulting in insufficient titer for forward processing downstream. Through data analysis and experimentation in controlled bioreactors, this poor performance has been linked to seed train culture conditions- primarily seed train culture pH. Standard manufacturing practices for pH monitoring and control were modified to more precisely control culture pH to desired set point. Non-standard metrics (such as cell size and oxygen uptake rate) have been used to monitor seed train cultures. Evidence of the poor growth phenotype can also be found in elevated levels of binding immunoglobin protein (BiP) in the seed train culture cells. With seed train pH control improvements and enhanced monitoring in place, the poor culture performance has not been observed in recent commercial campaigns.

In addition to reduced titer, product quality is also impacted when slower growth is observed in production culture, specifically out of specification high afucosylated species is observed. For one case of poor production performance that resulted in a high out of specification result for the afucosylated species, a review of equipment, cell age, raw material, adventitious agent testing, mechanical and process change records, and production media composition did not identify anything that could be linked to the slow growth observed. However, trend analysis revealed an abnormally high ammonium level in the early inoculum train stage. This case showed that minor deviations in the inoculum train cultures could result in poor performance in production cultures later, ultimately resulting in product quality failures. In order to reduce impact to product quality using this sensitive cell line, efforts to move the process into a more robust zone have been explored. Modified pH control strategies and impact to culture performance and product quality control will be discussed.